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NANOSYSTEMS IN CANCER THERAPY

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ABSTRACT

Nanomaterials of different chemical compostions, such as liposomes, micelles or inorganic nanoparticles hold tremendous potential as carriers for drugs to target cancer cells. The effectiveness of drug delivery systems can be attributed to their small size, reduced drug toxicity, controlled time release of the drug and modification of drug pharmacokinetics and biological distribution.

***KEYWORDS:** Nanomaterials, Liposomes, Cancer, Chemotherapeutics, Tumors*

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Original Article

INTRODUCTION

Cancer is the second leading cause of death next to cardiovascular diseases. An uncontrolled growth and multiplication of cells resulting into harmful tumor is called cancer. Cancer is characterized by the ability to invade adjacent tissues and even distant organs. It causes loss of cell differentiation, forms tumors, and interferes with normal body functions resulting in the death of affected persons if diagnosed very late. A tumor, caused by cancer is an abnormal mass of tissue formed as a result of excessive, uncoordinated, autonomous and purposeless proliferation of cells. There are two types of tumors, benign (eg. brain tumor) and malignant (breast cancer) tumor. Cancers are classified according to embryonic origin of the tissue from which the tumor is derived such as carcinomas, sarcoma, lymphomas, and leukemia. The environmental agents that cause cancer are known as carcinogens. It is not exactly known how a normal cell is converted into cancerous cell. The carcinogenic agents are responsible for causing malignant changes in the cell. There are different types of carcinogenic agents such as chemical carcinogens, radiations, biological agents, dietary factors, genetic factors and also cancers due to habits and customs. Cancer is being treated by surgery, radiation therapy, (such as gamma rays, x-rays, cobalt-60 and radium), chemotherapy (such as alkylating agents, anti-metabolites, antitumor antibiotic and plant alkaloids), immunotherapy. Mechanistic aspect of cancer and its therapy has been critically reviewed by Ji Luo *et al.* and Boyle and Costello [1-4]

Nanomaterials of different chemical compositions, such as liposomes, micelles or inorganic nanoparticles hold tremendous potential as carriers for drugs to target cancer cells. Several anti-cancer drugs including paclitaxel [5,6], doxorubicin [7], 5-fluorouracil [8]and

Dexamethasone[9] have been successfully formulated using nanomaterials. Polylactic/glycolic acid (PLGA) and polylactic acid (PLA) based nanoparticles have been formulated to encapsulate chemotherapeutic agent, dexamethasone [9]. The effectiveness of drug delivery systems can be attributed to their small size, reduced drug toxicity controlled time release of the drug and modification of drug pharmacokinetics and biological distribution. Too often, chemotherapy fails to cure cancer because some tumor cells develop resistance to

multipleanticancer drugs. In most cases, resistance develops when cancer cells begin expressing a protein, known as p-glycoprotein that is capable of pumping anticancer drugs out of a cell as quickly as they cross through the cell's outer membrane. New research shows that nanoparticles may be able to get anticancer drugs into cells without triggering the p-glycoprotein pump [6, 10.]

Targeting Cancer Cells with Nanoparticles

Cancer has remained the most dreadful disease till date. A variety of chemotherapeutics are available to deal with a variety of cancers. However, use of chemotherapy to target cancer not only kills cancer but also targets normal dividing cells of the body. Moreover, even the most potent therapeutic is rendered useless owing to its failure to reach the therapeutic target *in vivo*. Therefore, the need is to focus the research on targeted drug delivery which would only deliver the chemotherapeutics to cancerous cells while sparing the normal cells.

Recently researchers have started exploiting receptor mediated endocytosis to achieve a target specific drug delivery where the therapeutics can be targeted to the diseased tissue with the use of strategy of coupling therapeutics to certain molecules which have

Recognition by specific receptors present on the target tissue. Today with tremendous research being carried out on cancer, it has become evident that most cancers and their metastases over – express certain receptors, which act as potential drug target for cancer therapy. High levels of αhFR (folate receptors) are over expressed on a variety of human cancers like ovarian, breast, brain, lung and colorectal cancers but are restricted in normal tissues[11]. Internalization of folate hFR involves receptor mediated endocytosis. Consequently, several strategies have been developed for the targeted drug delivery or drugs to hFR - positive tumor cells. Covalent attachment of therapeutic agents to hFR targeted monoclonal antibodies have shown significant targeting efficiency in patients with ovarian cancer. Alternatively, folate derivatized anticancer treatments have been successfully applied *in vitro* for hFR-specific delivery. Evidence for overexpression of transferrin (a plasma glycoprotein) receptor on tumor cells including oral, prostrate and breast cancer cells implicate its role in target- specific delivery.

Lately, a new therapy called localized hyperthermia (also called local thermal therapy or thermotherapy) has shown promise in killing cancer cells. Hyperthermia is the application of concentrated therapeutic heat generated to treat cancer, which implies use of super paramagnetic iron oxide nanoparticles. In hyperthermia, desired body tissue is implanted with super paramagnetic iron oxide nanoparticles which are then super heated to high temperature (45^{o}C) by an external magnetic field (magnetic field hyperthermia). High temperature can damage and kill cancer cells, usually with minimal injury to normal tissues. In normal tissues, blood vessels dilate on heating. Unlike healthy cell, a tumor is a tightly packed group of cells in which circulation restricted and sluggish. When heat is applied to the tumor, vital nutrients and oxygen are cut off from tumor cells resulting in

Cell death owing to collapse of tumors vasculature. The super paramagnetic iron oxide nanoparticles used for hyperthermia are biodegradable and biocompatible and enhance the sensitivity of magnetic resonance imaging[12]. It has been observed that after intravenous injection, most super paramagnetic iron oxide nanoparticles accumulate in kuffer cells in the liver and in the reticuloendothelial system in the spleen. After being metabolized by cells, the iron is introduced in the normal plasma iron pool and can be incorporated into the hemoglobin of red

Cells and used in other metabolic processes. Dendrimer-coated super paramagnetic iron oxide nanoparticles (magneto dendrimers) have been used for cellular labeling.While ferum oxide, a dextran coated super paramagnetic iron oxide nanoparticles (FDA approved) have been used as MRI contrast agent for hepatic imaging.

Targeting Angiogenesis with Nanoparticles

Robust angiogenesis underlies aggressive growth of tumors. Therefore, one of the mechanisms to inhibit angiogenesis is to starve tumor cells. Angiogenesis is regulated through a complex set of mediators and recent evidence shows that integrin αvβ3 and vascular endothelial growth factors (VEGFs) play important regulatory roles. Therefore, selective targeting of αvβ3 integrin and VEGFs is a novel anti-angiogenesis strategy for treating a wide variety of solid tumors. One approach is to coat nanoparticles with peptides that bind specifically to the αvβ3 integrin and the VEGF receptor[13]. The synthetic peptide bearing Arg-Gly-Asp (RGD) sequence is known to specifically bind to the αvβ3 integrin expressed on endothelial cells in the angiogenic blood vessels, which can potentially inhibit the tumor growth and proliferation. Following hydrophobic

Modifications, glycol chitosan is capable of forming self-aggregated nanotube and has been used as a carrier for the RGD peptide, labelled with fluoresein isothiocyanate (FITC-GRGDS) [14].

Scientists at National Chemical Laboratory, Pune, India addressed the use of microorganisms such as fungi and plant extracts in the synthesis of nanomaterials, over a range of chemical compositions that includes metals, semi-conductors (quantum dots), alloys, oxides and bio-minerals. This opens up the exciting possibility of developing chemically and physically hard to synthesize inorganic nanomaterial such as oxide nanoparticles[15-18]. These oxide nanoparticles are important in applications such as hypothermia, drug delivery, targeted delivery etc. and are conventionally synthesized under harsh environments like extremes of temperature, pressure and pH. In contrast, biological processes occur under ambient conditions with room temperature, atmospheric pressure and physiological pH. Ansari *et al* synthesized CdS nanoparticles by enzymatic route and then coupled the nanoparticle with lectin[19].

CONCLUSIONS

The objective of this paper was to use of nanoparticles in cancer treatment. There is huge potential and global interest to use nanoparticles in cancer therapy. With intense in nanotechnology, it is likely that many of these questions will be addressed in the near future.

Conflict of Interest Statement

We declare that we have no conflict of interest.

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